UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,649	02/16/2006	Giorgio Terenghi	TEPH 109	4566

23579 7590 08/25/2010

Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER	
WANG, CHANG YU	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
08/25/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte GIORGIO TERENGHI, PARI-NAZ MOHANNA and
DAVID P. MARTIN

Appeal 2009-012878
Application 10/568,649
Technology Center 1600

Oral Hearing Held: July 22, 2010

Before ERIC B. GRIMES, LORA M. GREEN and JEFFREY N. FREDMAN,
Administrative Patent Judges

ON BEHALF OF THE APPELLANT:

PATRICIA PABST, ESQ.
Pabst Patent Group
1545 Peachtree Street, NE
Suite 320
Atlanta, Georgia 30309

THE USHER: Good morning. Public Calendar Number 37, Appeal Number 2009-012878, Appellant Giorgio Terenghi, Pabst Patent Group, LLP.

JUDGE GRIMES : Good morning.

MS. PABST: Good morning. And this is Dr. David Martin. He's one of the inventors from the assignee of the company. He's going to talk in just a minute., a very brief introduction, unless we appreciate the opportunity to be here and have a chance to discuss some of the issues.

What I'd like to do is let Dr. Martin talk for three or four minutes, just to generally talk about the technology, why the developed it amongst any problem in the field, and why do you suppose they were so unexpected. And then I'm going to talk about the legal errors that occurred in this case.

DR. MARTIN: Hello. I'm David Martin. I'm the VP of R&D at Tepha and I've been working with PHAs, which is a class of materials that we manufacture at Tepha for almost 20 years now. We started manufacturing these materials by cloning genes and putting them into microorganisms, so we created a cell that can function as a chemical engineering factory to make these polymers.

Originally, there was one polymer, poly3hydroxybutyrate that was used and there was extensive work done on that in the area of implantation, but it was found to be too crystalline, too stiff and slow absorbing to be useful in the late 90s when we first created this P4HB material. It was the first time it had ever been made and after testing amyls found that it could be useful for medical implants. It took us over 10 years to get the first medical device cleared through the FDA as a suture, and now we're beginning commercialization of a variety of medical implants based on

that material.

In early 2000 we started work on nerve guides with an expert in the field in the UK, Giorgio Terenghi, who had previously done work with the P3HB material and found that it didn't quite work as rapidly as would be necessary. So I created a foam of our new material, P4HB, that had pores in it and it could be rolled into a flexible tube, a hollow tube, to allow axonal growth across a nerve gap. And, originally when the experiment was set up, we picked end points of 10 and 20 days to observe the progression of nerve growth across the gap and unexpectedly, at the first explanation time point of 10 days the axon had already cleared the gap and this was much faster than he had previously observed with the other observable polymer, P3HB.

So that's when we knew we had found some interesting and unexpected results. And then we had followed, at later time points, with histology and observed the quality of nerve growth and subsequently filed a patent based on those findings. So there's been review papers published subsequent to that that suggest absorbable nerve guides are useful, and this type of application. But I don't think people have observed as quite as fast axonal regrowth as we observed in our initial studies. So at Tepha we're continuing to commercialize these materials and have been focusing on mostly tissue regeneration and wound closure devices. And now I'll try to commercialize that into that technology into a variety of different applications.

JUDGE GRIMES: Thank you.

MS. PABST: Again, what I'm going to do is just take a couple of minutes to go over what I think are some legal errors, and then if there are

any questions or issues. I think the first, major legal error that occurred in this case is that the examiner refused to consider the evidence. There are two actual groups of evidence.

The first is that in the application as filed we have a discussion of the prior art; and, in particular, we have a paper that was submitted in an information disclosure statement. And the examiner made it of record, and then when we cited this paper as showing comparative evidence, the examiner said she would not consider it even when in our reply brief we again established where this paper had been made of record.

JUDGE GRIMES: Which paper are you referring to?

MS. PABST: That is the Hazizi et al. paper.

JUDGE GRIMES: The Hazari reference?

MS. PABST: The "British Journal of Plastic Surgery;" the reason this paper was particularly important, it's cited in the application.

JUDGE GRIMES: I'm sorry. This is Hazari, British Journal of?

MS. PABST: Plastic Surgery.

JUDGE GRIMES: Plastic surgery. Okay. Thank you.

MS. PABST: Yes. Volume 52, 1999, the authors of this paper include one of the inventors of this application, and that's Dr. Terenghi. This is the work that Dr. Martin just discussed with respect to the P3HB. In the application as filed we reference this paper and provide a summary of the results. Now, there were two differences between the material that is described in this paper and in what is claimed. The first is that that paper used P3HB, and we claim P4HB or P4HB copolymer.

Second, none of the prior art, but in particular the nerve tube

used and described in this paper was porous, and this claim "porous P4HB nerve guide." So we have two differences that in the materials that were used in the two studies. The studies with the porous P4HB nerve guide are described in the application in example 5 at pages 9 to 10. So we think it was legal error that the examiner refused to consider the closest prior art, which was the P3HB without pores, and P4HB with pores, and the results.

If one reads the paper and the example, not only do we have a common inventor and author, but in fact it is the identical animal model and conditions used for the two situations: the rat's severed sciatic nerve, neural tube put in place, and then the results that she think compared. What was surprising to everybody was the fact that if you look at the papers cited by the examiner, these are subsequent reviews. And this is another thing she found to consider.

She cited two papers as being subsequent reviews. Clavijo Alvarez in the PRS Journal, "Plastic Reconstructive Surgery Journal," and she cited Schlosshauer -- and I don't know how to pronounce these names. I apologize -- in the "Journal of Neurosurgery." And both of them say that there was a need to have nerve guides that could encourage neuronal regeneration that approached that of an allograft and then all of the synthetic guides had to fail to reach that goal. That included the P3HB of Hazizi. So we have in the application as filed evidence that shows that in fact this nerve guide made of P4HB and porous can achieve that rate of axonal regeneration.

We show that by the first time, 10 days, we had already seen nerves completely close this gap. That had never been observed in any synthetic nerve guide prior to this example. It approaches the rate of an

allograft for nerve regeneration. In the field of nerves and in all of the papers cited by the examiner show this, that that rate of neuronal regeneration is critical to outcome.

We have longstanding, as established by the evidence the examiner cited, we have unexpected results here because we see axonal regeneration approaching that of an allograft. There is no prior art that gives you any indication that you could achieve that. If I am a patient who has had severed nerve, and particularly if it's a fairly long gap, that rate of regeneration is critical.

Now, there are other errors that we think the examiner made. Not only did the examiner refuse to consider the evidence of record, but a number of misstatements are made with respect to the references that she cited. I actually went through, as I'm sure you all have done, because neither tests this, gone through and looked at the places where she cites support for a number of her statements about what's shown in the prior art. And, I have to be honest. I have never seen this before.

The references she cites simply do not support her statements. She makes statements that are not only unsupported but they were contradicted by the passages that she actually cites, which is unusual. To give you an example, she makes reference to "Neuro Tube," which is one of the prior art nerve regeneration guides, which is also discussed in her reviews. And she says it shows a porous neuro tube. It does not show a porous neuro regeneration tube. It shows a material having microparticles in the material. That's not a pore. It's a micro particle. It is the antithesis of what we claim.

If you take the material that we're claiming, lay it on a napkin

and pour fluid on top, the fluid will pass through, important self regeneration. It allows free diffusion of those nutrients and gas to support the viability of that nerve cell. If you take a solid material, it does not. Having micro-particles in that structure may provide benefits since it's collagen and BCM. But it does not allow free diffusion. So not only is it not the same, it doesn't achieve the same goal.

So we have a number of differences there. We have no prior art showing a porous nerve tube. Now, when one looks at the prior art that was cited, in particular, Tepha's own earlier applications, there is a clear teaching that P4HB is a wonderful polymer. There's no dispute. And that there's a long list of materials that we might believe we make out of this. But those materials, such as the nerve guides, are not porous. There's no disclosure in any prior art reference of a porous nerve guide.

In fact, there's a teaching away, because they are solid polymers, the tubes. They are not porous materials. So even if you put all that prior art in combination, you would not have a P4HB porous nerve guide. You would have a teaching away from it. Now, one of the reasons for this is because those polymers don't have the mechanical properties of P4HB. So I think, again, we have prior art that doesn't disclose each claimed element. We have unexpected results. We have longstanding, but unmet, need. I think every one of these are the criteria the Supreme Court laid out in "John Deere" and "KSR" for non-obviousness. And I think we have legal error by the examiner in refusing to consider the evidence showing those things.

JUDGE GRIMES: I don't read the examiner as having not considered your evidence of unexpected results. She says that it's not

persuasive because it's not a side-by-side comparison.

MS. PABST: Well, first off, the examiner is incorrect in that statement, because in fact it was done by the same person with the same animal model under the same conditions, the examiner never looked at. However, I believe that if you looked at what the examiner actually says in her, it's hard to take and know what the examiner is saying, because she starts out with why she won't consider the evidence.

And then when she gets to the end, she says, well, it's not the same. The reason she says it's not the same is because she did not in fact read the evidence before her. We had two interviews in this case with the supervisor present, and he encouraged her to look at the evidence.

JUDGE GRIMES: Okay. Well, we have the evidence and they are similar experiments.

MS. PABST: They actually were done under the same conditions with the same model. And I know that I'm not going to --

JUDGE FREDMAN: When was this? They're not exactly the same. There's a little bit of everything.

MS. PABST: Well, the materials are different, but it was the same. Dr. Terenghi performed the experiments described in the Blue Book by Hazizi using a rat sciatic model and with a ten millimeter.

JUDGE FREDMAN: But you're giving us information that is in the record. At least it's not clear that Dr. Terenghi exhibited both of them himself. For the record, I don't think that -- says that.

MS. PABST: Well, I don't think there's any requirement, but the legal requirement that the same person do the studies. It is the same animal

model. It is the same size gap. It is the same general concept. The materials are clearly different. That's, of course, the whole point.

JUDGE GRIMES: Our problem here is that even if it's the same experiment that is being done by different people at different times, you might get somewhat different results.

MS. PABST: Well, in fact, by virtue it being an animal model, you can never have identical conditions. I think the standard is what do those skilled in the art think of those results. This was not a single example as you can see from Example 5 in the application.

Several different forms of these materials were tested across the board with the porous P4HB made under four different conditions. You see the same results. They are statistically, significantly, better than what is in any of the prior art, even in the reference cited by the appellants here Hazizi et al., or in any of the reviews cited by the examiner, which are later in date to applicant's work.

If you look at, for example, Ms. Schlosshauer that she cites, here is the 2007 part, 2006 paper. So three years after our prior art where they review all of these materials, and they don't even come close to achieving the results achieved by the appellants with their material using four different samples, multiple rat models. So, yes, there are some differences, but across the board it is statistically, significantly better. It meets that longstanding need, and it's the same animal model. And, if you look at Schlosshauer, who is one of probably far greater than ordinary skill in the art, in his review he feels very comfortable comparing results with far greater animal models in drawing these conclusions.

JUDGE GRIMES: And you made the point earlier that the goal was to get an artificial material that would replicate or that would approach the rate of regeneration of an axonal graft. Is that correct?

MS. PABST: Of an allograft.

JUDGE GRIMES: An allograft?

MS. PABST: Yes. That is the standard Schlosshauer.

JUDGE GRIMES: And the result in your specification, they don't include the results from the autologous nerve graft control. But it is those who understand --

MS. PABST: It's not a control. It's in the literature.

JUDGE GRIMES: No. It's not in the spec as well, and the results are presented for the P4HP sample, but they're not compared to the autologous nerve graft. I'm reading from the specification.

JUDGE FREDMAN: But we receive autologous nerve grafts.

MS. PABST: Right.

JUDGE FREDMAN: In our graft, right?

MS. PABST: Yes.

JUDGE FREDMAN: So that data is not presented.

JUDGE GRIMES: So my question to you is the expectation that those autologous nerve graft animals would have bridged the gap at the 10-day mark when the P4HB?

DR. MARTIN: Yes, it's possible that an allograft or an autologous graft could achieve that, but there are disadvantages with using -- especially autologous graft -- because that needs to be harvested from the patient. And so you suffer morbidity at the site and you might lose feeling.

So there are disadvantages to using autologous nerve grafts. And with allografts you always have the possibility of disease transmission because it's coming from another human.

So the move in the industry is to use a synthetic material where you don't have these other disadvantages and achieve the same axonal regeneration as the gold standard, which would be those autologous or allografts.

JUDGE GRIMES: All right.

MS. PABST: I don't think in our case. I don't think we've ever claimed it was the same. I think we used language like approaching. And the point is compared to the prior art it's almost a log factor better.

JUDGE FREDMAN: The other question I had is you recognized that your was better.

MS. PABST: I'm sorry. I'm having a little trouble hearing you.

JUDGE FREDMAN: The other question that I have is your claim, Claim 1 in particular, it seems that it encompasses not just a hydroxybutyrate, but also copolymers.

MS. PABST: It does.

JUDGE FREDMAN: So is it commensurate in scope with the results, which are limited, for hydroxybutyrate?

MS. PABST: Well, as I pointed out in my reply brief, to the extent the examiner never raised that as an issue. If it were raised, we do have our Claim 3, where we had tried to correct it upon the examiner would enter it. But again Claim 3 is limited to the homopolymer. And so if that had been raised as an objection, which it wasn't, we felt that Claim 3 addressed that.

So, and actually, to be honest, we would be happy with that, because that is what is being developed clinically and commercially. Because best results are with the homopolymer, that is what the FDA has approved.

As Dr. Martin was saying, the first synthetic polymer approved by the FDA in like 20, 30 years was the P4HB. So the FDA recognized that this was a very special polymer and that's what's actually being developed. So we wouldn't have a problem with that.

JUDGE GRIMES: I think we understand your position, or the unmarked -- of that.

MS. PABST: Thank you, so much.

Whereupon, at 9:23 a.m., the proceedings were concluded.